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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,752	08/19/2003	David R. Liu	LS5-001	4082

51414 7590 03/28/2007

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/643,752	Applicant(s) LIU ET AL.	
	Examiner Stephanie K. Mummert, Ph.D.	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-48 and 104* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-48 and 104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/22/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on December 22, 2006 is acknowledged and has been entered. Claims 24 and 37 have been amended. Claims 1-23 and 49-103 have been canceled. Claims 24-48 and 104 are pending.

Claims 24-48 and 104 are discussed in this Office action.

All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This action is made FINAL.

Previous Rejections

The rejection of claims 24-28 and 104 under Obviousness Double Patenting is withdrawn in view of Applicant's abandonment of the 10/949162 application. The Obviousness Double Patenting rejection of claims 24, 30-31, 36-37, 41 and 104 in view of application 10/101030 has been amended to a non-provisional rejection in light of the patenting of this application (now 7,070,928). The rejection of claims 24, 30-37, 41-48 and 104 under 35 U.S.C. 102 as being anticipated by Sergeev is withdrawn in view of Applicant's amendment the claims. A new ground of rejection under 35 U.S.C. 103 has been applied. The rejection of claims 24-40 under

35 U.S.C. 102 as being anticipated by Koster and the rejection of claims 25-29 and 38-40 under 35 U.S.C. 103 as being unpatentable over Sergeev and Koster is withdrawn.

Information Disclosure Statement

1. The information disclosure statements (IDS) submitted on December 22, 2006 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 24, 30-31, 36-37, 41 and 104 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 36-37, 39-41 and 49 of US Patent 7,070,928 (issued July 4, 2006; '928 patent herein) in view of Sergeev. Although the

conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application and the '928 patent are drawn to a method wherein a template directs the synthesis of a reaction product, through the binding of transfer units to anti-codon sequences within the template and with reactive units attached to the transfer units.

The claims differ from one another in that the claims of the instant application are directed to a method of increasing reaction selectivity among multiple reactants and it is not explicitly stated within the claim that the method is carried out *in vitro*. However, the method steps of the instant application accomplish nucleic acid templated synthesis, in addition to increasing reaction selectivity. Furthermore, the specification of the instant application discloses that the method may be performed *in vitro*.

Finally, while claim 47 of the copending application is directed specifically to a reaction between first and second reactive units, and claims 24, 37 and 104 recite up to three or four reactive units, considering claim 49, a plurality of reactive units and a plurality of templates may be incorporated into the method of producing different reaction products. Therefore, it would be obvious to incorporate more than the first two reactive units into the method described in the instant application and the '928 patent. Furthermore, considering the teaching of Sergeev, wherein a plurality of transfer units with a plurality of reactive units are contemplated for template directed synthesis reactions (p. 15 top diagram where up to 'n' oligomer transfer units are disclosed). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to extend the broad teachings of claim 49 of the '928 patent, in light of the teachings of Sergeev to arrive at the claims of the instant application.

4. Claims 24-28 and 104 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 47-48 and 54 of copending Application No. 11/586851. Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of the copending application represent a broader scope of the claims of the instant application.

In the copending application, the claims are directed to a method for the synthesis of a library of chemical compounds comprising steps wherein a plurality of templates, a plurality of reactive units and a plurality of transfer units are incorporated in the method. In the instant application, a specific combination of transfer units and reactive units are claimed which are used in a method of template directed synthesis wherein the reaction selectivity is enhanced. The inclusion of multiple reactive units and transfer units within the claims of the instant application would fall within the scope of the plurality of components claimed in the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

5. Claims 24-28 and 104 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 47 and 64 of copending Application No. 10/949163. Although the conflicting claims are not identical, they are not patentably distinct. The claims of the copending application differ from the claims of the instant application in that the claims of the copending application are amended to explicitly claim that the method of synthesis is directed to the formation of a small molecule and the claims incorporate small molecule scaffolds in place of the term 'reactive unit' in the instant

application. However, while the term 'reactive unit' is not given an explicit definition, the term is taught as "a reactive unit (e.g., a scaffold molecule)" (paragraph 11 of PgPub of instant application), therefore, it would be obvious that a small molecule comprising small molecule scaffolds and building blocks would result from the practice of the method claimed in the instant application and in the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Interpretation

The term 'reactive unit' is being given the broadest reasonable interpretation in light of the specification. As the term is not explicitly defined and is instead referred to in terms such as "a reactive unit (e.g., a scaffold molecule)" (paragraph 11 of PgPub). While this term "scaffold molecule" is defined as "a chemical compound having at least one site or chemical moiety suitable for functionalization. The small molecule scaffold or molecular scaffold may have two, three, four, five or more sites or chemical moieties suitable for functionalization. These functionalization sites may be protected or masked as would be appreciated by one of skill in this art. The sites may also be found on an underlying ring structure or backbone." (paragraph 42 of PgPub).

Also, it is not clear from the specification that the term does not encompass nucleotides or nucleic acid molecules, the term is being interpreted broadly as encompassing nucleic acid templated synthesis techniques which include ligation reactions between nucleotides.

Claim Rejections - 35 USC § 103

1. Claims 24-48 and 104 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sergeev (WO00/61775; October 2000) in view of Gartner and Liu (Journal of the American Chemical Society, 2001, vol. 123, p. 6961-6963, as evidenced by supporting documentation. Sergeev teaches a method of syntheses of biologically active substances based on the hybridization of two or more oligomers which are bound with biologically active precursors which interact to form a biologically active substance (Abstract).

With regard to claim 24, Sergeev teaches a method of increasing reaction selectivity among a plurality of reactants in a nucleic acid-templated synthesis to produce a reaction product that is not a nucleic acid, the method comprising the steps of:

(a) providing (i) a template comprising a first reactive unit associated with a first oligonucleotide comprising a predetermined codon sequence, (ii) a first transfer unit comprising a second reactive unit associated with a second oligonucleotide comprising an anti-codon sequence capable of annealing to said codon sequence, and (iii) a second transfer unit comprising a third reactive unit different from said second reactive unit associated with a third oligonucleotide without an anti-codon sequence capable of annealing to said codon sequence (p. 11-17, where the binding of multiple transfer units capable of binding to a template with separate codon sequences are present are linked to multiple reactive units; see also Figures 1-10 and p. 21-24, where the Figures are described); and

(b) mixing said template, said first transfer unit and said second transfer unit under conditions to permit annealing of said second oligonucleotide of said first transfer unit to said first oligonucleotide of said template thereby to enhance covalent bond formation between said

second reactive unit and said first reactive unit relative to covalent bond formation between said third reactive unit and said first reactive unit to produce the reaction product (p. 11-17, where the binding of multiple transfer units capable of binding to a template with separate codon sequences are present are linked to multiple reactive units; see third step where a chemical bond forms between reactive units).

With regard to claim 37, Sergeev teaches a method of increasing reaction selectivity among a plurality of reactants in a nucleic acid-templated synthesis to produce a reaction product that is not a nucleic acid, the method comprising the steps of:

(a) providing (i) a template comprising a first oligonucleotide comprising first and second codon sequences, (ii) a first transfer unit comprising a first reactive unit associated with a second oligonucleotide comprising a first anti-codon sequence capable of annealing to said first codon sequence, (iii) a second transfer unit comprising a second reactive unit associated with a third oligonucleotide comprising a second anti-codon sequence capable of annealing to said second codon sequence, and (iv) a third transfer unit comprising a third reactive unit associated with a fourth oligonucleotide sequence without an anti-codon sequence capable of annealing to said first codon sequence or said second codon sequence (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to respective reactive units); and

(b) mixing said template, said first transfer unit, said second transfer unit and said third transfer unit under conditions to permit annealing of said first anti-codon sequence to said first codon sequence and said second anti-codon sequence to said second codon sequence thereby to enhance covalent bond formation between said first reactive unit and said second reactive unit relative to covalent bond formation between said third reactive unit and said first reactive unit or

between said third reactive unit and said second reactive unit to produce the reaction product (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to respective reactive units; see step where chemical bond is formed between reactive units).

With regard to claim 30, Sergeev teaches an embodiment of claim 24, wherein said first reactive unit is covalently attached to said first oligonucleotide (p. 11-17, where the binding of multiple transfer units capable of binding to a template with separate codon sequences are present are linked to multiple reactive units; see p. 11-17, where the linking moieties are described and wherein these moieties covalently link the reactive unit to their respective oligomer).

With regard to claim 31 and 41, Sergeev teaches an embodiment of claim 24 and 37, wherein said second reactive unit is covalently attached to said second oligonucleotide (p. 11-17, where the binding of multiple transfer units capable of binding to a template with separate codon sequences are present are linked to multiple reactive units;.see p. 11-17, where the linking moieties are described and wherein these moieties covalently link the reactive unit to their respective oligomer).

With regard to claim 32 and 42, Sergeev teaches an embodiment of claim 24 and 37, wherein said third reactive unit is covalently attached to said third oligonucleotide (p. 11-17, where the binding of multiple transfer units capable of binding to a template with separate codon sequences are present are linked to multiple reactive units; see p. 11-17, where the linking moieties are described and wherein these moieties covalently link the reactive unit to their respective oligomer).

With regard to claim 33, Sergeev teaches an embodiment of claim 24, wherein said second reactive unit and said third reactive unit are capable of reacting independently with said first reactive unit (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to respective reactive units, where first and second reactive units are capable of reacting, p. 15, and wherein first and third reactive units are capable of reacting – see Figure 4).

With regard to claim 34, Sergeev teaches an embodiment of claim 24, wherein said second reactive unit and said third reactive unit are capable of reacting with one another (see p. 15, for example, where the second and third reactive units react with one another).

With regard to claim 35, Sergeev teaches an embodiment of claim 34, wherein the reaction between said second reactive unit and said third reactive unit are incompatible with their respective reactions with said first reactive unit (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to respective reactive units, where first and second reactive units are capable of reacting, p. 15, and wherein first and third reactive units are capable of reacting – see Figure 4).

With regard to claim 36, Sergeev teaches an embodiment of claim 24, comprising providing a plurality of transfer units (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to respective reactive units and where 'n' is a plurality of transfer units).

With regard to claim 43, Sergeev teaches an embodiment of claim 37, wherein said third reactive unit is covalently attached to said fourth oligonucleotide (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to respective reactive units

and where the linking moieties are described and wherein these moieties covalently link the reactive unit to their respective oligomer).

With regard to claim 44, Sergeev teaches an embodiment of claim 37, wherein said third reactive unit is capable of reacting with said first reactive unit or said second reactive unit (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to respective reactive units, where second and third reactive units are capable of reacting, p. 15, and wherein first and third reactive units are capable of reacting – see Figure 4).

With regard to claim 45, Sergeev teaches an embodiment of claim 37, wherein said third reactive unit is capable of reacting with said first reactive unit and said second reactive unit (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to respective reactive units, where second and third reactive units are capable of reacting, p. 15, and wherein first and third reactive units are capable of reacting – see Figure 4).

With regard to claim 46, Sergeev teaches an embodiment of claim 44 or 45, wherein the reaction between said third reactive unit and said first reactive unit is incompatible with the reaction between said first reactive unit and said second reactive unit (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to respective reactive units, where second and third reactive units are capable of reacting, p. 15, and wherein first and third reactive units are capable of reacting – see Figure 4).

With regard to claim 47, Sergeev teaches an embodiment of claim 44 or 45, wherein the reaction between said third reactive unit and said second reactive unit is incompatible with the reaction between said first reactive unit and said second reactive unit (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to respective reactive units,

where second and third reactive units are capable of reacting, p. 15, and wherein first and third reactive units are capable of reacting – see Figure 4).

With regard to claim 48, Sergeev teaches an embodiment of claim 37, wherein said covalent bond formation between said first reactive unit and said second reactive unit is via a regioselective distance dependent reaction (p. 15, for example, where it is noted that the distance between oligomers is between 0 to 7 nucleotides; Figure 1, where the reaction is selective in that the reactive units have to be in the proper selective position for reaction to occur).

With regard to claim 104, Sergeev teaches an embodiment of claim 24, further comprising:

providing a second template comprising a fourth reactive unit associated with a fourth oligonucleotide comprising a second predetermined codon sequence, different from said predetermined codon sequence of said first oligonucleotide, wherein said second predetermined codon sequence is capable of annealing with said third oligonucleotide; and

mixing said second template with said first transfer unit, said second transfer unit, and

said template comprising said first reactive unit associated with said first oligonucleotide under conditions to permit annealing of said second oligonucleotide of said first transfer unit to said first oligonucleotide of said template and, in the same solution, annealing of said third oligonucleotide of said second transfer unit to said fourth oligonucleotide of said second template, thereby to induce covalent bond formation both between said second reactive unit and said first reactive unit and between said fourth reactive unit and said third reactive unit (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to respective reactive units; see step where chemical bond is formed between reactive units,

including a reaction between first and second reactive units and between third and fourth reactive units).

Regarding claims 24 and 37, Sergeev does not teach that the method can be practiced in vitro. Gartner teaches a related method and discloses the use of the method in vitro to analyze the reaction products, to generate a library using in vitro synthesis.

With regard to claims 24 and 37, Gartner and Liu teach an in vitro method of increasing reaction selectivity (throughout disclosure, particularly as disclosed and described at Figures 1-7, specifically, Figures 6 and 7 describe in vitro selection of a library; see also supporting information published with the original article that discloses that the DNA-templated synthesis reactions were carried out in vitro through the mixing of equimolar quantities of reagent and template in buffer containing 50 mM MOPS, pH 7.5 and 250 mM NaCl at the desired temperature).

With regard to claims 25 and 38, Gartner and Liu teach an embodiment of claim 24 and 37, wherein said template is associated with a capturable moiety (Figure 6, where the template is associated with a capturable moiety).

With regard to claim 26-27, Gartner and Liu teaches an embodiment of claim 24, wherein said first transfer unit is associated with a capturable moiety (Figure 6, where the oligonucleotide transfer unit is associated with a capturable moiety).

With regard to claim 28 and 39, Gartner and Liu teaches an embodiment of claim 25, 26, 27 or 38 wherein said capturable moiety is selected from the group consisting of biotin, avidin and streptavidin (Figure 6, where the capturable moiety is exemplified as biotin, selected through binding to streptavidin coated beads; see also p. 6962-3).

With regard to claim 29, Gartner and Liu teaches an embodiment of claim 28, further comprising the step of capturing said capturable moiety (Figure 6, where the template associated with the biotin after reaction is 'in vitro selected' through capture with streptavidin beads).

With regard to claim 40, Gartner and Liu teaches an embodiment of claim 38, wherein said capturable moiety is a reaction product resulting from a reaction between said first reactive unit and said second reactive unit when said first transfer unit and said second transfer unit are annealed to said template (Figure 6, where the biotin capturable moiety is a product of the reaction between the template and the first reactive unit).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the technique of template-directed synthesis of molecules, including RNA, proteins and small molecules as taught by Sergeev to include the technique and method in an in vitro format as taught by Gartner and Liu to arrive at the claimed invention with a reasonable expectation for success. As taught by Gartner and Liu, "We are interested in creating amplifiable and evolvable libraries of non-natural small molecules by developing methods to translate DNA into synthetic structures. Achieving this goal requires using DNA to direct chemical reactions sequence-specifically in a manner much more general than has been reported thus far" and "we examined the ability of two DNA architectures to support solution-phase DNA-templated synthesis" (p. 6961, col. 1). Gartner and Liu conclude "these findings indicate that DNA-templated synthesis is general phenomenon capable of supporting a range of reaction types and is not limited to the creation of structures resembling nucleic acid backbones" (p. 6961, col. 1-2). Throughout Gartner and Liu, the method is clearly practiced in vitro and in the supporting materials provided with the publication, the DNA templated synthesis reactions

were practiced wherein equimolar quantities of reagent and template in a buffer, followed by the removal and analysis of aliquots by denaturing PAGE electrophoresis (p. 1 of supporting information). While the specific DNA-template structures are slightly different than the format disclosed by Sergeev, clearly both methods share a common theme of using DNA templates to direct the synthesis of non-nucleic acid molecules and Gartner and Liu also establish that the method can be practiced in vitro and that the in vitro method can be used as a "basis for translating the amplifiable information in a library of DNA into non-natural synthetic small molecules in one pot, as demonstrated by the translation, selection, and amplification of the model synthetic library described" (p. 6963, col. 2). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have also practiced the method of the invention in vitro in order to achieve isolation of the products of the synthesis reaction with a reasonable expectation for success.

New Grounds of Rejection as necessitated by Applicant's amendment to the claims

2. Claims 24, 30-34, 36-37, 41-45, 47-48 and 104 are rejected under 35 U.S.C. 102(b) as being anticipated by Dorner et al. (Journal of Virology, 1984, vol. 50, no. 3, p. 507-514) as evidenced by Brooker (Genetics Analysis and Principles, 1999, edition 1, Menlo Park, CA). Dorner teaches a method of in vitro translation of poliovirus RNA in reticulocyte lysate samples (Abstract).

With regard to claim 24, Dorner teaches a method of increasing reaction selectivity among a plurality of reactants in a nucleic acid-templated synthesis, the method comprising the steps of:

(a) providing (i) a template comprising a first reactive unit associated with a first oligonucleotide comprising a predetermined codon sequence, (ii) a first transfer unit comprising a second reactive unit associated with a second oligonucleotide comprising an anti-codon sequence capable of annealing to said codon sequence, and (iii) a second transfer unit comprising a third reactive unit different from said second reactive unit associated with a third oligonucleotide without an anti-codon sequence capable of annealing to said codon sequence (p. 509, 'cell-free protein synthesis' heading, where reticulocyte lysate and HeLa cell extract were used for in vitro protein translation, where rabbit liver tRNA was added and where the reaction products were labeled with 35S-methionine; see also p. 326, 368 of Brooker, where the individual tRNAs have an anticodon sequence and an attached amino acid which is specific for the anticodon; see p. 326, where it is noted that there are 64 different codons and 20 amino acids, therefore there are at least three reactive units with specific anticodon sequences attached); and (b) mixing said template, said first transfer unit and said second transfer unit under conditions to permit annealing of said second oligonucleotide of said first transfer unit to said first oligonucleotide of said template thereby to enhance covalent bond formation between said second reactive unit and said first reactive unit relative to covalent bond formation between said third reactive unit and said first reactive unit (p. 509, 'cell-free protein synthesis' heading, where reticulocyte lysate and HeLa cell extract were used for in vitro protein translation, where rabbit liver tRNA was added and where the reaction products were labeled with 35S-methionine).

With regard to claim 37, Dorner teaches a method of increasing reaction selectivity among a plurality of reactants in a nucleic acid-templated synthesis to produce a reaction product that is not a nucleic acid, the method comprising the steps of:

(a) providing (i) a template comprising a first oligonucleotide comprising first and second codon sequences, (ii) a first transfer unit comprising a first reactive unit associated with a second oligonucleotide comprising a first anti-codon sequence capable of annealing to said first codon sequence, (iii) a second transfer unit comprising a second reactive unit associated with a third oligonucleotide comprising a second anti-codon sequence capable of annealing to said second codon sequence, and (iv) a third transfer unit comprising a third reactive unit associated with a fourth oligonucleotide sequence without an anti-codon sequence capable of annealing to said first codon sequence or said second codon sequence (p. 509, 'cell-free protein synthesis' heading, where reticulocyte lysate and HeLa cell extract were used for in vitro protein translation, where rabbit liver tRNA was added and where the reaction products were labeled with 35S-methionine; see p. p. 326, where the process of translating a specific sequence is diagrammed; where the oligonucleotide has more than only a first and second codon sequence, and where there are more than three transfer units with reactive units (amino acids) attached); and

(b) mixing said template, said first transfer unit, said second transfer unit and said third transfer unit under conditions to permit annealing of said first anti-codon sequence to said first codon sequence and said second anti-codon sequence to said second codon sequence thereby to enhance covalent bond formation between said first reactive unit and said second reactive unit relative to covalent bond formation between said third reactive unit and said first reactive unit or between said third reactive unit and said second reactive unit to produce the reaction product (p. 509, 'cell-free protein synthesis' heading, where reticulocyte lysate and HeLa cell extract were used for in vitro protein translation, where rabbit liver tRNA was added and where the reaction

products were labeled with 35S-methionine, wherein the reaction product is a protein; see explanation of codon and anti-codon sequences as described by Booker above).

With regard to claim 30, Dorner teaches an embodiment of claim 24, wherein said first reactive unit is covalently attached to said first oligonucleotide (p. 373 of Booker, Figure 14-3, where the reactive unit (amino acid) is attached to the tRNA oligonucleotide, and where the linkage between the oligonucleotide and the reactive unit is covalent).

With regard to claim 31 and 41, Dorner teaches an embodiment of claim 24 and 37, wherein said second reactive unit is covalently attached to said second oligonucleotide (p. 373 of Booker, Figure 14-3, where the reactive unit (amino acid) is attached to the tRNA oligonucleotide, and where the linkage between the oligonucleotide and the reactive unit is covalent).

With regard to claim 32 and 42, Dorner teaches an embodiment of claim 24 and 37, wherein said third reactive unit is covalently attached to said third oligonucleotide (p. 373 of Booker, Figure 14-3, where the reactive unit (amino acid) is attached to the tRNA oligonucleotide, and where the linkage between the oligonucleotide and the reactive unit is covalent).

With regard to claim 33, Dorner teaches an embodiment of claim 24, wherein said second reactive unit and said third reactive unit are capable of reacting independently with said first reactive unit (p. 326 of Booker, where the process of translating a specific sequence is diagrammed; where the oligonucleotide has more than only a first and second codon sequence, and where there are more than three transfer units with reactive units (amino acids) attached; it is

also noted that any of the transfer units is capable of reacting with the first reactive unit, depending only on the sequence of the codon present in the template).

With regard to claim 34, Dorner teaches an embodiment of claim 24, wherein said second reactive unit and said third reactive unit are capable of reacting with one another (p. 326 of Booker, where the process of translating a specific sequence is diagrammed and where it is noted that the binding of tRNAs with specific anticodons bind to the codon sequence in a sequential manner, therefore the second and third units are capable of and should react with one another).

With regard to claim 36, Dorner teaches an embodiment of claim 24, comprising providing a plurality of transfer units (p. 509, 'cell-free protein synthesis' heading, where reticulocyte lysate and HeLa cell extract were used for in vitro protein translation, where rabbit liver tRNA was added and where the reaction products were labeled with 35S-methionine; where as evidenced by p. 326, a plurality of transfer units are included in the reaction).

With regard to claim 43, Dorner teaches an embodiment of claim 37, wherein said third reactive unit is covalently attached to said fourth oligonucleotide (p. 373 of Booker, Figure 14-3, where the reactive unit (amino acid) is attached to the tRNA oligonucleotide, and where the linkage between the oligonucleotide and the reactive unit is covalent).

With regard to claim 44, Dorner teaches an embodiment of claim 37, wherein said third reactive unit is capable of reacting with said first reactive unit or said second reactive unit (p. 326 of Booker, where the process of translating a specific sequence is diagrammed and where it is noted that the binding of tRNAs with specific anticodons bind to the codon sequence in a sequential manner, therefore the second and third units are capable of and should react with one another).

With regard to claim 47, Dorner teaches an embodiment of claim 44 or 45, wherein the reaction between said third reactive unit and said second reactive unit is incompatible with the reaction between said first reactive unit and said second reactive unit (p. 326 of Booker, where the process of translating a specific sequence is diagrammed and where it is noted that the binding of tRNAs with specific anticodons bind to the codon sequence in a sequential manner, therefore the second and third units are capable of and should react with one another after the first and second units react with one another).

With regard to claim 48, Dorner teaches an embodiment of claim 37, wherein said covalent bond formation between said first reactive unit and said second reactive unit is via a regioselective distance dependent reaction (p. 379 of Booker, Figure 14-9, where the process of translation is depicted more broadly and where it is also clear that the bond formation between any reactive unit is a regioselective distance dependent reaction; insofar as an amino acid will only be added to the growing peptide when the proper tRNA binds the appropriate anticodon in the template).

With regard to claim 104, Dorner teaches an embodiment of claim 24, further comprising:

providing a second template comprising a fourth reactive unit associated with a fourth oligonucleotide comprising a second predetermined codon sequence, different from said predetermined codon sequence of said first oligonucleotide, wherein said second predetermined codon sequence is capable of annealing with said third oligonucleotide; and

mixing said second template with said first transfer unit, said second transfer unit, and said template comprising said first reactive unit associated with said first oligonucleotide under

conditions to permit annealing of said second oligonucleotide of said first transfer unit to said first oligonucleotide of said template and, in the same solution, annealing of said third oligonucleotide of said second transfer unit to said fourth oligonucleotide of said second template, thereby to induce covalent bond formation both between said second reactive unit and said first reactive unit and between said fourth reactive unit and said third reactive unit (p. 509, 'cell-free protein synthesis' heading, where reticulocyte lysate and HeLa cell extract were used for in vitro protein translation, where rabbit liver tRNA was added and where the reaction products were labeled with 35S-methionine; see p. p. 326, where the process of translating a specific sequence is diagrammed; where the oligonucleotide has more than only a first and second codon sequence, and where there are more than three transfer units with reactive units (amino acids) attached; and where it is also noted that the reticulocyte lysate would not comprise only a single nucleic acid sequence as depicted in Brooker; multiple templates would be translated, with multiple transfer units or tRNAs, simultaneously).

Response to Arguments

6. Applicant's arguments filed December 22, 2006 have been fully considered but they are not persuasive.

Applicant's arguments with respect to claims 24, 30-37, 41-48 and 104 have been considered but are moot in view of the new ground(s) of rejection. However, insofar as the arguments apply to the new grounds of rejection, the arguments will be addressed.

Applicant asserts that Sergeev discloses a method of synthesizing a biologically active substance directly in the cells of living organisms. Applicant's arguments have been considered and the amendment to the claims has necessitated a new grounds of rejection under 35 U.S.C. 103 as recited above.

Applicant also asserts that "the Sergeev method (see for example Figure 1), does not use a template (e.g., the cellular RNA or DNA) comprising a first reactive unit" and "Sergeev fails to teach or suggest an in vitro method that uses 'a second transfer unit comprising a third reactive unit different from said second reactive unit associated with a third oligonucleotide without an anticodon capable of annealing to said codon sequence'" (see p. 8-9 of remarks). These arguments are not persuasive because Applicant has not provided any detail or explanation in support of these assertions, either referring back to Applicant's disclosure or to specific portions of the Sergeev reference. Without more detailed arguments in support of these assertions, it is not possible to rebut the assertion, beyond stating that these arguments are found unpersuasive for the reasons provided in the newly cited 103 rejection stated above. In particular,

Finally, regarding Applicant's request that the Obviousness Double Patenting rejections be held in abeyance, Applicant's arguments are fully considered and found unpersuasive because these are not the only remaining rejections in this application. As discussed above, the rejections under 35 U.S.C. 103(a) are still pending. Thus, the rejections under provisional double patenting are maintained until the issues are resolved.

Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. include Landegren et al. (Science, 1988, vol. 241, no. 4869, p. 1077-1080) teaches an assay for the detection of a specific DNA sequence based on the ability of oligonucleotides to anneal adjacent to one another on a target DNA molecule (Abstract). Bruick et al. (Current Biology, 1996, vol. 3, p. 49-56) describe a method for chemical ligation of peptides to oligonucleotides in a template directed reaction (Abstract). Summerer and Marx (Angew. Chem. Int. Ed. 2002, vol. 41, no. 1, p. 89-90) review the field of DNA templated synthesis (Schemes 1-4 and Figure 1).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie K. Mummert, Ph.D. whose telephone number is 571-272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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